Recreating the perivascular niche ex vivo using a microfluidic approach.

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Public Summary:

Scientific Abstract:
Stem cell niches are composed of numerous microenvironmental features, including soluble and insoluble factors, cues from other cells, and the extracellular matrix (ECM), which collectively serve to maintain stem cell quiescence and promote their ability to support tissue homeostasis. A hallmark of many adult stem cell niches is their proximity to the vasculature in vivo, a feature common to neural stem cells, mesenchymal stem cells (MSCs) from bone marrow and adipose tissue, hematopoietic stem cells, and many tumor stem cells. In this study, we describe a novel 3D microfluidic device (MFD) as a model system in which to study the molecular regulation of perivascular stem cell niches. Endothelial cells (ECs) suspended within 3D fibrin gels patterned in the device adjacent to stromal cells (either fibroblasts or bone marrow-derived MSCs) executed a morphogenetic process akin to vasculogenesis, forming a primitive vascular plexus and maturing into a robust capillary network with hollow well-defined lumens. Both MSCs and fibroblasts formed pericytic associations with the ECs but promoted capillary morphogenesis with distinct kinetics. Biochemical assays within the niche revealed that the perivascular association of MSCs required interaction between their alpha6beta1 integrin receptor and EC-deposited laminin. These studies demonstrate the potential of this physiologically relevant ex vivo model system to study how proximity to blood vessels may influence stem cell multipotency.